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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 40

Application Number: 08/253,973
Filing Date: 06/03/94
Appellant(s): McBride et al.

Patricia McDaniels
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed 09/09/99.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 3-7 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

5,688,485	HARRIS	11-1997
5,091,514	FRITZBERG ET AL.	2-1992

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harris (USP 5,688,485) in view of Fritzberg (USP 5,091,514).

Harris discloses ligands having the formula as shown in column 3, wherein Z is an amino group of the formula, R_{17}-N-R_{18}, yields ligands having the donor set SNNN or NNNS (stereoisomeric forms, see column 4, lines 40-45). The formula substituted wherein, R_6 together with R_7 and R_{13} together with R_{14}, to form an oxygen atom (see column 3, lines 57 and 60) and the remaining R_1-R_{18} groups are substituted with H, alkyl moieties, etc., would yield compounds within the scope of the ligands of the instant claims, except for such compounds would not include a linker and targeting moiety, as instantly claimed. The ligands form complexes with various radiometals, such as Tc-99m, etc. for use as radioimaging agents, see column 4, lines 1-14.

Fritzberg discloses ligands which may have the donor set SNNN which are used as radiopharmaceuticals for methods of diagnosis or therapy. Fritzberg teaches that such ligands may be conjugated to a targeting compound to provide the advantage of being able to specifically deliver the ligands to a target site *in vivo* for methods of diagnosis or therapy, see columns 6-7. The targeting agents may be conjugated to various substituents of the ligands and may include a linking moiety to facilitate the conjugation of the targeting moiety, see column 7, lines 41+. The linker may form an amide linkage with a polypeptide (e.g., as encompassed by the instant claims), see column 8.

Since Harris and Fritzberg both disclose ligands and radiometal complexes thereof having the same utility as radioimaging and/or radiotherapeutic agents, they may be viewed as being in the same field of endeavor.

Although Harris may not disclose that the ligands may be conjugated to a targeting agent or that such conjugation may be through a linker, it would have been obvious to one of ordinary skill in the art to conjugate a targeting agent to the ligands disclosed by Harris using a linker (e.g., amide, etc.) because it is well known in the art that ligands may be conjugated to various targeting via various linking moieties, such as amide linkage to a peptide, to improve the biodistribution of the ligand for use as an imaging agent, as shown by Fritzberg.

(11) Response to Argument

Appellant's arguments filed 09/09/99 have been fully considered but they are not persuasive.

Appellant asserts that the examiner has ignored limitations which are expressly stated in the prior art. More specifically that the examiner has ignored the disclosure of "diaminethiol" in Harris, while the instant claims are directed toward monoamine, diamide, single thiol-containing ligands (and not diamine).

This is not found persuasive because Harris discloses ligands having a formula which encompasses ligands having the donor set SNNN or NNNS (stereoisomeric forms) which may be monoamine, diamide, single thiol-containing ligands and within the scope of the instant claims. Harris discloses that the "preferred" compounds are a "diaminedithiol" (e.g., see column 4, line 59-60), however, the formula which is disclosed by Harris clearly encompasses monoamine, diamide, single thiol ligands which are similar to those instantly claimed (e.g., only excluding a targeting moiety). Although the preferred embodiments of the Harris invention may be diamine or diaminedithiol, there are no provisos set forth in the description of the formula which limit the formula to such compounds. Thus, the disclosure of Harris teaches monoamine, diamide thiol containing ligands. Disclosed examples and preferred embodiments do not constitute a teaching which is away from a broader disclosure or nonpreferred embodiments. *In re Susi, 169* USPQ 423 (CCPA 1971) and *In re Gurley*, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994).

Appellant appears to assert that the formula disclosed by Harris is limited to "diaminethiols" because of this term is expressly stated in the reference. However, this cannot be

the case since Harris specifically disclosed compounds which are not "diaminethiols" and are encompassed by the disclosed formula. For example, compounds XVII (column 8) XIX (column 9) are specifically disclosed species' which are not diaminethiols, but which are encompassed by the formula shown in column 3. Since Harris discloses a general formula with specific substitutions, the entire genus of the formula is taught by Harris. Furthermore, the express statement of Harris of "diaminethiol" appears to describe the general formula having at least two nitrogen atoms and one sulfur, SNN(S or N) ligands as shown by the formula in column 3. However, Harris clearly teaches that various R groups may form an oxygen atom, which would change the amine to an amide. This is clear from the formula as shown. One of ordinary skill in the art would have recognized that the disclosure of Harris teaches all the ligands within the scope of the disclosed formula. A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 10 USPQ2d 1843 (Fed. Cir. 1989).

Appellant asserts that the cited case law, e.g., *In re Susi, 169* USPQ 423 (CCPA 1971); *In re Gurley*, 31 USPQ2d 1130, 1132, Fed. Cir. 1994 and *Merck & Co. v. Biocraft Laboratories*, 10 USPQ2d 1843 (Fed. Cir. 1989), is incorrectly applied because in each of these cases the invention actually fell within the genus described in the prior art.

This is not found persuasive because the general formula disclosed by Harris may be substituted to yield ligands which are monoamine, diamide, single thiol-containing ligands, which are within the scope of the claimed chelator.

Appellant asserts that Harris teaches away from the instantly claimed chelators because the chelators in Harris are expressly described as diaminethiols, diaminedithiols or diamidedithiols.

This is not found persuasive because although Harris exemplifies diaminethiols, diaminedithiols or diamidedithiols and mentions that diaminedithiols are preferred, the formula disclosed by Harris clearly encompasses chelators which are monoamide, diamide, thiols. As stated above, preferred embodiments and disclosed examples do not constitute a teaching away from a broader disclosure. For example, if the recitation of "diaminethiol" in describing the general formula in column 3 is expressly limiting, it would not be possible for Harris to disclose "diamidedithiols" which are set forth in examples. Thus, the teaching of Harris is only limited to the compounds encompassed by the formula set forth in column 3.

In response to appellant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Harris discloses ligands which are used as radiopharmaceuticals and it is well known in the art that such radiopharmaceutical chelating agents may be conjugated to a targeting moiety to provide the advantage of *in vivo* site-specificity of the chelant as shown by Fritzberg. One of ordinary skill in the art would have been motivated to conjugate a targeting moiety to the

chelants disclosed by Harris, by known methods of conjugating a targeting agent to gain the advantage of site specificity, as taught by Fritzberg. Since Harris and Fritzberg both disclose chelating agents having the same utility as radiopharmaceuticals, they are in the same field of endeavor. One of ordinary skill in the art would have been motivated to consider all of the prior art in the field of radiopharmaceuticals, such as, Harris and Fritzberg, and combine the teaching to provide the advantages gained therefrom. This would include the well-known advantages gained from conjugating a targeting ligand to such chelators as taught by Fritzberg, in the chelators disclosed by Harris.

Appellant asserts that the combination of Harris and Fritzberg is inoperative because the antibodies, antibody fragments, etc. disclosed by Fritzberg would be expected to accumulate in the kidneys.

This is not found persuasive because Fritzberg teaches that various targeting moieties may be used and conjugated to ligands. The targeting moieties bind to various desired sites, such as cancer cells, etc. (see columns 8-9) and would therefore be expected to provide the advantage of site-specificity to various desired sites.

Appellant asserts that the combination of Harris and Fritzberg does not yield a proper combination because the formula disclosed by Harris, when modified by those disclosed by Fritzberg does not include the compounds instantly claimed.

This is not found persuasive because Fritzberg is not being used to modify the basic formula of Harris to arrive at monoamine, diamine, thiol chelators as instantly claimed. As set

forth, such ligands are encompassed and taught by the formula disclosed by Harris. Fritzberg is being used to show that it is known in the art that such radiopharmaceutical ligands may be conjugated to such radiopharmaceutical chelators as various positions, via various linkers to provide the advantage of site specificity.

In response to appellant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the appellant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The conjugation of a targeting agent to a ligand is well known in the art, only taking into account knowledge which was within the level of ordinary skill at the time of the invention, as shown by Fritzberg. In order to rely on a reference as a basis for rejection of an appellant's invention, the reference must either be in the field of appellant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). See also *In re Deminski*, 796 F.2d 436, 230 USPQ 313 (Fed. Cir. 1986); *In re Clay*, 966 F.2d 656, 659, 23 USPQ2d 1058, 1060 - 61 (Fed. Cir. 1992). Since Harris and Fritzberg both disclose similar chelators which are used for radiopharmaceuticals, they are in the same field of endeavor. Fritzberg teaches that the

knowledge of conjugating a targeting moiety to various positions of a chelator via a linker to provide *in vivo* site specificity, was within the level of ordinary skill at the time the claimed invention.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

JOSE G. DEES
SUPERVISORY PATENT EXAMINER
1616

MH
October 5, 1999

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